Patent Claims

- Process for preparing levosalbutamol or the pharmacologically acceptable salts thereof starting from prochiral salbutamone as educt, characterised in that salbutamone is subjected to asymmetric hydrogenation in the presence of rhodium and a chiral bidentate phosphine ligand as catalyst system, and the levosalbutamol obtained is optionally converted into a salt with an acid.
- 2. Process according to claim 1, characterised in that the ligand is (2R, 4R)-4-(dicyclohexylphosphino)-2-(diphenylphosphino-methyl)-N-methyl-aminocarbonyl-pyrrolidine.
- 3. Process according to claim 1, characterised in that the ligand is polymer-bound (2R, 4R)-4-(dicyclohexylphosphino)-2-(diphenylphosphino-methyl)-N-methyl-aminocarbonyl-pyrrolidine.
- 4. Process according to one of claims 1 to 3, characterised in that the asymmetric hydrogenation is carried out in a temperature range from 20°C to 100°C.
- Process according to claim 4, characterised in that the asymmetric hydrogenation is carried out in a temperature range from 40°C to 60°C.
- 6. Process according to claim 5, characterised in that the asymmetric hydrogenation is carried out in a temperature range from 45°C to 55°C.
- 7. Process according to one of the preceding claims 1 to 6, characterised in that the asymmetric hydrogenation is carried out under a pressure of more than 1 bar to 100 bar, preferably under a pressure of 10 bar to 50 bar.
- 8. Process according to claim 7, characterised in that the asymmetric hydrogenation is carried out under a pressure of about 20 bar.

- 9. Process according to one of the preceding claims 1 to 8, characterised in that the asymmetric hydrogenation is carried out in a protic solvent.
- Process according to claim 9, characterised in that the asymmetric hydrogenation is carried out in a branched or unbranched C₁ – C₈alkanol as solvent.
- 11. Process according to the preceding claim 10, characterised in that the asymmetric hydrogenation is carried out in methanol, ethanol, n-propanol and/or isopropanol as solvent.
- 12. Process according to one of the preceding claims 9 to 11, characterised in that the solvent for the asymmetric hydrogenation contains water.
- 13. Process according to one of the preceding claims 1 to 12, characterised in that during asymmetric hydrogenation salbutamone is used in a molar ratio to the rhodium catalyst of from 500:1 to 100000:1, preferably from 750:1 to 20000:1.
- 14. Process according to claim 13, characterised in that the molar ratio of salbutamone to the rhodium catalyst during asymmetric hydrogenation is about 1000:1.
- 15. Process according to one of the preceding claims 1 to 14, characterised in that the rhodium catalyst for the asymmetric hydrogenation is used as a pre-prepared solution.
- 16. Process according to one of the preceding claims 1 to 14, characterised in that the rhodium catalyst for the asymmetric hydrogenation is produced in situ.

- 17. Process according to one of the preceding claims 1 to 16, characterised in that the asymmetric hydrogenation is carried out within a reaction time of 2 to 48 hours, preferably 4 to 36 hours.
- 18. Process according to claim 17, characterised in that the reaction time for the asymmetric hydrogenation is about 23 hours.
- 19. Process according to one of the preceding claims 1 to 18, characterised in that salbutamone is prepared starting from N-benzylsalbutamone by hydrogenation in the presence of a palladium catalyst.
- 20. Process for preparing levosalbutamol or the pharmacologically acceptable salts thereof, which comprises the following steps:
- (a) brominating 4-acetyloxy-3-acetyloxymethylbenzophenone,
- (b) reacting the product obtained with N-tert-butyl-N-benzylamine,
- (c) hydrogenating the N-benzylsalbutamone obtained in the presence of a palladium catalyst,
- (d) hydrogenating the salbutamone obtained in the presence of rhodium and a chiral bidentate phosphine ligand, and
- (e) optionally treating it with an acid.